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Original Article

Pattern of coagulation in pediatric and adult multiple trauma patients

Yusuf Kenan Tekin[2], Neslihan Yucel[1]

[2]Cumhuriyet University, Medical of Medicine, Department of Emergency Medicine, Sivas, Turkey
[1]Inonu University, Medical of Medicine, Department of Emergency Medicine, Malatya, Turkey

Abstract

Aim: Aim of this study was evaluated changes in coagulation parameters in adult and pediatric multiple trauma patients.
Material and Methods: A prospective observational study was conducted of adult and pediatric patients with blunt multiple trauma. The platelet count, prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), fibrinogen, D-dimer, tissue factor (TF), factor VII and factor X were evaluated.
Results: For our pediatric trauma patients, platelet count, factor VII and factor X were inversely related to the APACHE II score, whereas aPTT, D-dimer and INR and APACHE II scores were positively correlated. Furthermore, we found that aPTT, D-dimer, INR and TF in adults positively correlated with the APACHE II score. We also found that factor X, aPTT, and platelet count were strongly associated with adverse outcomes in pediatric trauma patients, and remained independently associated in the multivariate analysis.
Conclusion: TF and INR are strongly associated with adverse outcomes after multiple traumas in adults. However, in pediatric patients, platelet count, aPTT, TF and factor X are associated with adverse outcomes. Therefore, early assessment of TF and INR in adult trauma patients, and platelet count, aPTT, TF and factor X in pediatric trauma patients, may significantly improve the accuracy of assessments of the severity of traumatic injuries.

Keywords: Coagulopathy; clotting factors; posttraumatic coagulopathy; trauma.

INTRODUCTION

CCoagulopathy is a common occurrence, present in approximately one-third of major trauma patients arriving at the emergency department (ED) (1,2). Moreover, it is associated with an almost four-fold increase in mortality in this patient population (3). Trauma-induced coagulopathy and bleeding have a multifactorial etiology and are a common problem after severe injury in pediatric and adult patients. Coagulopathy is a preventable cause of death in trauma patients, and managing coagulopathy. Also, the presence of coagulopathy upon admission to the ED before massive fluid administration is associated with injury severity and significantly higher mortality (4,5).

Posttraumatic activation of the coagulation system in response to tissue destruction plays a major role in critically injured and bleeding patients (6,7). The management of trauma-induced coagulopathy in patients with multiple traumas requires rapid and adequate decisions, given the potentially lethal complications. Trauma-induced coagulopathy can be initially investigated according to various parameters including prothrombin time (PT), activated partial thromboplastin time (aPTT), thrombin time, fibrinogen level, platelet count, D-dimer level, and blood viscoelastic tests of clotting amplitude and clot lysis (1-9).

Several severity scoring systems such as Glasgow Coma Scale (GCS), Injury Severity Score (ISS), and new injury severity score (NISS), have been developed for ED, pre-hospital setting and intensive care unit (ICU) to gauge the severity of injury, triage and predict death risk (10-13). In contrast, the APACHE II system was designed to prognosticate mortality and severity of illness in all critical patients according to physiological variables during the first 24 hour after ICU admission (12).

Aim of this prospective study is to evaluated patterns of coagulation in early stage of trauma for both adult and

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Corresponding Author: Neslihan Yucel, Inonu University, Medical of Medicine, Department of Emergency Medicine, Malatya, Turkey
E-mail: nesyucel@hotmail.com

pediatric severe trauma patients. Our secondary goal is to evaluate the relationship between APACHE II and coagulation parameters within the trauma groups.

MATERIAL and METHODS

Study design and setting

Between June 2010 and May 2011, we enrolled 70 consecutive multiple trauma patients (35 adults aged ≥18 years and 35 children aged <18 years) who were admitted to the ED of Inonu University hospital. The Institutional Review Board of Inonu University approved the prospective observational study design. The authors had complete access to the medical information of all participants, which was stored anonymously in a database.

Patients were included if they had been directly transferred to our ED within 1 hour of the traumatic event, had injuries to at least two systems or an Injury Severity Score (ISS) ≥16, and were not administered blood, blood products, or any fluid. Patients were excluded if they had ISS scores <16 or single-system injuries, or if they received any fluid infusions. Patients who arrived at the ED more than 2 hours after leaving the scene of the incident, and those that received care at another medical center, were also excluded from the study. The relatives of study subjects completed an informed consent form and were provided with updates until hospital discharge or in-hospital death.

All blunt multiple trauma patients were monitored and vital signs including blood pressure, pulse rate, respiratory rate, body temperature, and pulse oximetry values were recorded. Patients were rapidly examined, and pediatric and adult GCS values were determined. Blood samples were drawn to measure hemoglobin, hematocrit, platelet count, aPTT, international normalized ratio (INR), d-Dimer, fibrinogen, blood type, tissue factor (TF), factor VII and factor X values at the time of two large intravenous line placement, before intravenous infusion therapies.

Patients were managed according to Advanced Trauma Life Support (ATLS) guidelines. All patients received the required care their physical, radiological, and laboratory findings necessitated. Patient data was recorded including age, gender, trauma mechanism, duration in the ED, respiratory rate, heart rate, blood pressure, sites of the injuries (head and neck, abdomen, chest, pelvis, extremities), radiological findings, the clinic of admission, preferred treatment (surgical, conservative), duration of hospitalization, mortality rate, and the patients' trauma score values at time of presentation to ED [GCS, ISS, and Pediatric Trauma Score (PTS)]. The severity of injury in multi trauma patients was initially determined using the APACHE II score.

Statistical analyses

The SPSS for Windows software package (ver. 15.0; SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. Descriptive statistics were calculated, including mean, standard deviation (SD), and frequency. Categorical data were compared using the chi-square or Fisher's exact test. Depending on whether the data were normally distributed, continuous data were compared using either the unpaired t-test or Mann-Whitney U-test. The relationships among the variables were determined using Pearson's correlation coefficient. A multivariate logistic regression analysis (backward-stepwise test) was used to assess the APACHE II score. A p-value of ≤0.05 was considered statistically significant. Estimated odds ratios (ORs) and their corresponding 95% confidence intervals (CIs) were calculated.

RESULTS

AA total of 70 trauma cases were included in this study, consisting of 56 (80%) males 14 (20%) females. The average patient age was 22.9±19.0 years (range: 1-71 years). Mean ISS score was 38±11 in pediatric multiple trauma (PMT) group and 37±10 in adult multiple trauma (AMT) group. Additionally, mean GCS was 12±3 in PMT group and 11±4 in AMT group. Pediatric trauma score was 5±4 for children.

Demographics and injury characteristics of the study population are presented in Table 1. Among the multiple trauma patients, there were 23 (33%) cases of car accidents and 23 (33%) of fall-related injuries. Multiple trauma cases were significantly more common among the adults than the children (51%, vs. 11% p=0.002). The overall mortality rate of our cohort was 18.6 % (Table 1).

The hematologic and coagulation parameters, and the APACHE II scores, of the study participants are summarized in Table 2 for PMT and adult multiple trauma AMT groups. Differences in platelet counts, fibrinogen levels and APACHE II scores were observed. Platelet counts were higher in the PMT group compared to the AMT group (289.4±86.3 vs. 223.7 ± 80.9, p<0.001), whereas the fibrinogen levels and APACHE II scores were higher in the AMT group than the PMT group (521.5±167.9 vs. 342.8±143.9, p<0.002; and 13.6±8.2 vs. 11.2±8.4, p=0.037, respectively).

Correlations between coagulation characteristics and APACHE II scores in both the pediatric and adult study populations are presented in Table 3. Levels of hemoglobin and hematocrit, and platelet counts, were strongly and negatively correlated with the APACHE II scores in the PMT group (r= -0.664, p<0.001; r= -0.666, p<0.001; and r= -0.519, p=0.001, respectively). The levels of aPTT, INR and D-dimer were strongly and positively correlated with the APACHE II scores in both the PMT and AMT group (r= 0.887, p<0.001; r= 0.878, p<0.001; and r= 0.399, p=0.017 in the PMT group; and r= 0.455, p=0.006; r= 0.586, p<0.001; and r=0.495, p=0.003 in the AMT group, respectively). Also, TF was strongly and positively correlated with the APACHE II score in the AMT group (r= 0.413, p=0.014), while factor VII and factor X levels were strongly and negatively correlated with the APACHE II scores in the PMT group (r=-0.477, p=0.004; and r=-0.553, p=0.001, respectively).

As presented in Table 4, multivariate regression analysis of coagulation markers in the PMT group showed that platelet count, aPTT , TF and factor X level independently predicted the APACHE II score (β=-0.21, p=0.006; β=0.73, p<0.001; β=0.15, p=0.035; and β= -0.17, p=0.032, respectively), whereas INR and TF were the most significant predictors of the APACHE II scores in the AMT group (β=0.60, p<0.001; and β=0.42, p=0.001, respectively).

Table 1. Characteristic of the study participants based on children versus adults.

	All patients (n=70)	Children (n=35)	Adults (n=35)	p Value (Chi-square test)
Gender				
Male	56 (80.0)	28 (80.0)	28 (80.0)	NS
Female	14 (20.0)	7 (20.0)	7 (20.0)	
Mechanism of injury				
Fall	23 (32.9)	13 (37.1)	10 (28.3)	0.016*
Pedestrian accident	14 (20.0)	11 (31.4)	3 (9.2)	
Motorcycle or bicycle crash	10 (14.2)	5 (14.2)	5 (14.2)	
Car accident	23 (32.9)	6 (17.3)	17 (48.3)	
Injured body region				
Head and neck	24 (34.3)	15 (42.9)	9 (25.7)	0.002*
Thorax	5 (7.1)	2 (5.7)	3 (8.6)	
Abdomen, lower back and pelvis	13 (18.6)	8 (22.96)	5 (14.3)	
Extremities	6 (8.6)	6 (17.1)	-	
Multiple body region	22 (31.4)	4 (11.4)	18 (51.4)	
Signs of life on arrival				
Present	57 (81.4)	30 (85.7)	27 (77.1)	NS
Absent	13 (18.6)	5 (14.3)	8 (22.9)	

*Fisher exact test

Table 2. Hematologic and coagulation characteristics and trauma scores of the study participants based on children versus adults.

	All patients (Mean±SD)	Children (Mean±SD)	Adults (Mean±SD)	p (t test)
Hemoglobin (g/dL)	11.8 ± 2.2	11.5 ± 1.9	12.2 ± 2.5	NS
Hematocrit (%)	34.9 ± 5.5	33.9 ± 5.3	36.0 ± 5.6	NS
Platelet (103 cells/mm3)	256.6 ± 89.5	289.4 ± 86.3	223.7 ± 80.9	<0.001
aPTT (sec)	41.8 ± 36.0	37.3 ± 29.4	46.2 ± 41.5	NS
International normalized ratio	1.6 ± 1.3	1.8 ± 1.8	1.5 ± 0.5	NS
D-dimer (mg/L)	17.3 ± 12.9	16.4 ± 14.0	18.2 ± 11.7	NS
Fibrinogen (mg/dL)	432.2 ± 179.4	342.8 ± 143.9	521.5 ± 167.9	<0.001
Tissue factor	284.5 ± 81.4	281.5 ± 65.6	287.6 ± 95.5	NS
Factor VII	97.0 ± 31.7	94.8 ± 24.3	99.1 ± 38.0	NS
Factor X	99.4 ± 27.3	97.9 ± 21.4	100.9 ± 32.4	NS
APACHE II	12.4 ± 8.4	11.2 ± 8.4	13.6 ± 8.2	0.037

aPTT: Activated partial thromboplastin time; APACHE II: Acute Physiology and Chronic Health Evaluation

Table 3. Correlation between coagulation variables and the APACHE II scores in patients.

	Children (n= 35)		Adults (n= 35)	
	R	p	R	p
Hemoglobin (g/dL)	-0.664	<0.001	-0.276	0.109
Hematocrit (%)	-0.666	<0.001	-0.236	0.173
Platelet (mm3/dL)	-0.519	0.001	-0.133	0.447
aPTT (sec)	0.887	<0.001	0.455	0.006
International normalized ratio	0.878	<0.001	0.586	<0.001
D-dimer (mg/L)	0.399	0.017	0.495	0.003
Fibrinogen (mg/dL)	-0.179	0.302	0.220	0.204
Tissue factor	0.134	0.442	0.413	0.014
Factor VII	-0.477	0.004	-0.064	0.715
Factor X	-0.553	0.001	-0.098	0.574

aPTT: Activated partial thromboplastin time; APACHE II: Acute Physiology and Chronic Health Evaluation

Table 4. Stepwise multiple regression analysis of coagulation markers in patients.

APACHE II (Children)	B	p
Independent variables		
Platelet (mm3/dL)	-0.21	0.006
aPTT (sec)	0.73	<0.001
Tissue factor	0.15	0.035
Factor X	-0.17	0.032
APACHE II (Adults)		
Independent variables		
International normalized ratio	0.60	<0.001
Tissue factor	0.42	0.001

aPTT: Activated partial thromboplastin time; APACHE II: Acute Physiology and Chronic Health Evaluation

DISCUSSION

Multiple intrinsic mechanisms enable to stop bleeding in patients with trauma after injury, including thrombin-mediated clot formation, platelet aggregation, and vasoconstriction. Failure of one o more coagulation mechanisms exacerbates blood loss, and exsanguination cause to be a significant source of early death after injury (14). This study evaluates the coagulation parameters and the relationship between apache II score and coagulation parameters in adult and pediatric multiple trauma patients who were admitted to ED.

Coagulopathy may result from hypoperfusion, which is compounded by hypothermia and acidosis, and from direct tissue injury and consumption of clotting factors through hemorrhage and haemodilution (6). It is known that coagulopathy presence upon ED before massive fluid administration and associated with injury severity and significantly higher mortality in adult trauma patient (4,5,7,15). In contrast to adults, massive bleeding in children is very rare post-trauma, and traumatic brain injury appears to be the common trigger of trauma-induced coagulopathy and mortality (16).

Trauma-induced coagulopathy is multifactorial and involves all components of the hemostatic system. Activation or dysfunction of fibrin generation or both, platelets, and endothelium each play a role, together with a relative inhibition of stable clot formation by anticoagulant and fibrinolytic pathways. Which of these mechanisms predominates depends on severity of tissue injuries, the degree of circulatory physiologic derangement, and the deleterious side effects of medical therapies (7,17-19). A better understanding of the posttraumatic coagulopathy system and its mechanisms has led to the development of new therapeutic approaches for treatment and aggressive management in adults. Although trauma-related coagulation has long been known to occur in children (20), the pediatric population represents an understudied group in the context of coagulation, with very few studies being reported to date (20-22). A study by Hendrickson et al. investigated trauma-related coagulation in pediatric trauma patients and found a high prevalence of coagulation abnormalities within the first 24 hours of admission (23). Hence, the assessment of coagulation status of more severely injured children is essential to improve pediatric trauma care (24).

The hemostatic roles of coagulation factors include three pathways which name is the intrinsic coagulation pathway, the extrinsic coagulation pathway, and the common coagulation pathway. Furthermore, PT and aPTT are known sensitive tests, which can reflect the exogenous and endogenous coagulation functions, and prolonged PT and aPTT value can suggest that the patient is in a hypercoagulable state, and indicate clotting mechanism disorder (25). Among many tests for clinically detecting the coagulation functions, the current most traditionally used parameters are platelet count, PT/INR, aPTT, and fibrinogen. Also, European clinical practice guideline recommended that routine practice include the early and repeated monitoring of coagulation, using either a PT/INR, aPTT, platelet counts, fibrinogen, or a viscoelastic method in management of major bleeding and coagulopathy (26).

The platelet count is within the normal range in the most trauma patient, and less than 5% of trauma patient had a platelet count of <100.000 /L at emergency department admission (27,28). Another study showed that platelet count decreased after trauma within 48 h and increased after that in an animal trial (7). In patients exhibiting traumatic coagulopathy, the platelet count does not decline to levels that might be expected to contribute significantly to coagulopathy (27,28). However, the platelet count on admission, may be predictive of outcome as documented in some cohorts of massively transfused trauma patients where platelet count was inversely correlated with injury severity, morbidity and mortality (29,30). We demonstrated that platelet count differs between pediatric and adult patients and it was higher in pediatric trauma patients than adults. In the present study, adult trauma patients the frequency of multiple body region injury was higher in adult patients than in pediatrics, possibly explaining the differences noted above.

In traumatic hemorrhage and trauma induced coagulopathy, fibrinogen plays a important role in maintaining effective hemostasis (31,32). It is critical in both primary hemostasis (platelet aggregation) and secondary hemostasis (it is cleaved by thrombin to form fibrin). Admission low fibrinogen level has been associated with the Injury Severity Score and shock, and is an independent predictor of mortality. In addition, low fibrinogen level was determined at admission and progressed with the coagulopathy process. Critical (≤1.0 g/L) and abnormal (1.0–1.8 g/L) fibrinogen levels were also reported in 21 and 44% of severe trauma patients who required massive transfusions, respectively (33). The present study demonstrated that in early period of trauma, fibrinogen levels were higher in adult trauma than pediatrics.

Despite the advances in trauma care over the last three decades, traumatic injuries are the leading cause of death for young individuals and and it is difficult to predict death in patients with multiple traumas. Consequently, several scoring systems have been developed for use in patient's triage, accurately quantify injury, evaluate outcome and evaluate therapeutic quality. (10,12,13). In the care of multiple trauma patients, accurate scoring systems would be of great value. APACHE II score which is widely used clinically as an internationally recognized system for evaluating the condition of critically ill patients can be used to perform more comprehensive assessments of the severity of the illness and to predict the patients' risk of hospital death after admission to intensive care unit (ICU) (12). Multiple trauma patients usually visit the ICU after resuscitation, emergency operation or intervention. Several studies investigated the outcome predictive abilities of APACHE II score and other trauma scoring systems in ICU trauma patients and APACHE II score was found to be good predictor of group mortality in ICU trauma patients (34-36).

Injury severity is positively associated with the development of acute traumatic coagulopathy in trauma patients (1,3). Disorders in blood coagulation have been commonly observed in trauma, and are associated with adverse outcomes in adults as well as childen (1,2,5,23). APACHE II score was not only good predictor in determining mortality but in determining the severity of injury as well. The usefulness of coagulation parameters for predicting possible outcomes in trauma patients has been investigated previously (2,23). Therefore, in this study, it was analyzed whether there was any relationship between APACHE II score and coagulation variables. In our study, the correlations between coagulation parameters and APACHE II scores in multiple trauma patients revealed that, for pediatric trauma patients, hemoglobin, hematocrit, platelet count, and factor VII and factor X levels were negatively related to the APACHE II score, while there was a positive relationship between the APACHE II score and aPTT, D-dimer and INR (where higher APACHE II scores are indicative of poorer outcomes). Furthermore, aPTT, D-dimer, INR and TF in adults were positively correlated with the APACHE II score. Therefore, this study supports that of Saggar et al., in which aPTT predicted adverse outcomes in the patients with severe injury (37).

We found that factor X, aPTT, and platelet count were strongly associated with adverse outcomes in pediatric trauma patients and remained independently associated in the multivariate analysis. Similar to this finding, previous studies reported that abnormal aPTT and platelet count were strongly associated with poor outcome in multivariate analysis after adjusting for ISS (21,31).

Limitations

The small number of multiple trauma patients enrolled in this prospective study may compromise the generalizability of our findings.

CONCLUSION

In this prospective study, coagulopathy factors were evaluated in adult and pediatric patients during the early stage of multiple trauma, and prior to fluid administration. Coagulopathy is prevalent in multiple trauma patients and is strongly associated with the APACHE II score. Multiple trauma patients with early admission to ED exhibit different degrees of coagulation abnormalities. TF and INR in adult patients, and platelet count, aPTT, TF and factor X in pediatric patients, are strongly associated with adverse outcomes after multiple traumas. Early measurement of TF and INR in adult trauma patients, and of platelet count, aPTT, TF and factor X in pediatric trauma patients, may significantly aid in initial assessments of injury severity. .

Competing interests: The authors declare that they have no competing interest.
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Yusuf Kenan Tekin ORCID: 0000-0001-8047-4836
Neslihan Yucel ORCID: 0000-0001-5845-2614

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